UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/076,727	02/13/2002	John T. Groves	IB-1695	2093

8076 7590 08/03/2005

LAWRENCE BERKELEY NATIONAL LABORATORY
ONE CYCLOTRON ROAD, MAIL STOP 90B
UNIVERSITY OF CALIFORNIA
BERKELEY, CA 94720

EXAMINER	
SHIBUYA, MARK LANCE	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 08/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/076,727	GROVES ET AL.	
	Examiner	Art Unit	
	Mark L. Shibuya	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *1-6 and 21-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/26/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-24 are pending. Claims 1-6 and 21-24 are withdrawn from consideration. Claims 7-20 are examined.

2. The applicant's Reply, entered 5/26/2005, has been considered. Rejections and/or objections not reiterated from the previous Office action, are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

Election/Restrictions

3. Applicant again traverses the restriction requirement between Groups I and II. Applicant argues that the claims in Group I are not drawn to the culture of cells. Applicant cites to MPEP 806.03 for language that the restriction apply to claimed inventions.

As stated in the previous Office action and restriction, this is not found persuasive because the specification as filed discloses that the product of Group I may be used to culture cells. The specification at para [0078], for example, states that cells may be cultured on the membranes of the claimed device. Claim 1 is drawn to a micro-array device for determining adherence of selected cells and claims lipid membranes in corrals for moving a plurality of cells. Although the claims are not drawn to a cell culture device, it is clear from applicant's specification that cells may be cultured on the device

of Group I. Restriction is over the claimed inventions. However, the claimed invention of Group I may be used for more than one purpose, even if that additional purpose is not claimed.

The requirement is still deemed proper and is therefore maintained as FINAL.

4. This application contains claims 1-6 and 21-24, drawn to an invention nonelected with traverse in the Paper entered 11/24/2004. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Priority

5. This application claims benefit of 60/269,625, filed 2/16/2001, and claims benefit of 60/296,952, filed 6/8/2001.

Information Disclosure Statement

6. The information disclosure statement filed 5/26/2005 fails to comply with 37 CFR 1.97(c) because it lacks a statement as specified in 37 CFR 1.97(e). Also, the information disclosure statement filed 5/26/2005 fails to comply with 37 CFR 1.97(c) because it lacks the fee set forth in 37 CFR 1.17(p). It has been placed in the application file, but the information referred to therein has not been considered.

Claim Rejections - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

7. Claims 7-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Kam et al., U.S. Publication No. 2002/0009807. This rejection maintains the reasons of record as set forth in the previous Office action.

The claims are drawn to methods for screening, determining or observing living cell adhesion comprising providing a micro-array device comprising membranes in corrals, contacting or culturing cells in the device, and determining adhesion of the cells to the membranes; and wherein the membranes are lipid bilayers, wherein the membranes are doped with negatively or positively charged lipids, wherein the membranes are separated from a solid substrate by a water layer, wherein the substrate is a micropatterned glass wafer; wherein the membrane is an egg-phosphatidylcholine membrane; and wherein the lipid is phosphatidylserine (elected species).

Kam et al., U.S. Publication No. 2002/0009807, throughout publication, and at para [0027] teach methods for detecting cell adhesion using lipid bilayers separated from a solid support by a layer of water several nanometers thick, so that molecular components in the lipid bilayers of appropriate composition freely diffuse within the plane of the membrane; at para [0029]-[0031], teach methods for micropatterning lipid bilayers in devices that facilitate adhesion of anchorage-dependent cells onto fluid membranes and at para [0047], [0051], teach barrier regions on the surface that surround regions for cell-adherence, which are "corrals" measuring 10 micrometer or 20 micrometer in width, but not 40 microns in width, so that cells may randomly sample membrane "elements" before adhering to one and that would prevent diffusion between the membranes of distinct corrals; at para [0061-[0062], teach cell adhesion experiments wherein cow pulmonary arterial endothelial cells were allowed to adhere for 6 hours to substrates with arrays of lipid corrals; at para [0030], [0058] teach devices having a plurality of distinct bilayer-compatible surface regions composed of different materials, and separated by one or more bilayer barrier regions and micropattern geometries in a regular array of squares measuring either 5, 10, 20, 40 micrometers in width (which reads on microarrays); at [0047], wherein the substrate is glass; at para [0040], at para [0048], teach membranes of bilayers of egg phosphatidylcholine and, at [0060] teach egg phosphatidylcholine membranes supplemented with a negatively charged phospholipid that is Texas Redo 1,2-dihexadecanoyl-sn-glycero-3-phosphoethanolamine (TR-PE).

Applicant argues that the applicant teaches selective adhesion to lipid bilayers, while Kam teaches no adhesion to the lipid bilayer. Applicant argues that Kam only teaches cell adhesion to the protein fibronectin, deposited on the substrates, and not to the lipid expanse above the substrate.

Response to Arguments

Applicant's arguments entered 5/26/2005 have been fully considered but they are not persuasive.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., methods of cell adhesion to lipid bilayers) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The claims are drawn to screening for living cell adhesion, or to methods for determining cell adhesion. The reference of Kam teaches screening for cell adhesion to a lipid membrane; the result of that screening is that cells do not adhere to the lipid membrane of Kam (see, e.g., Figures 2). In a method for screening for a result, as in the claimed methods, observance of a negative result still falls within the metes and bounds of the claimed method. The claims do not require that the cells adhere to the lipid membrane, i.e., a positive result, even if the instant specification teaches such a positive result.

8. Claims 7, 8, 14, 15, and 16 are rejected under 35 U.S.C. 102(e) as being anticipated by Chen et al., US Publication No. 2002/0182633. This rejection maintains the reasons of record as set forth in the previous Office action.

Chen et al., U.S. Publication No. 2002/0182633, throughout the publication, and especially at para [0012], at teach methods of observing and screening cell adhesivity or attachment, comprising biomolecules, including lipids, (specification at para [0022], [0066]) on glass substrates for use in microarray analysis; at para [0073] wherein the spatially patterned surfaces have areas that are adhesive to cells and areas that do not bind cells, and wherein the cell adhesive areas form islands that are isolated by cytophobic regions to which cells do not adhere (reading on corrals separated by barrier) and wherein the islands may have a lateral dimension of between 0.2 and 10 microns; at para [0102], teach lipid bilayers; at para [0109] teach allowing cells to attach for 2 hours; at para [0123] teach the visual assays for determining cell adhesion; and at para [0119] teach using glass wafers as supports.

Applicant argues that PEO lipid bilayers, as taught by the reference of Chen, are not claimed in the applicant's application. Conversely, the applicant's lipid bilayers floating within corrals are not described by the reference of Chen. Instead, Chen et al. generally appears to bind selectively only directly to substrates, not to any lipid bilayers. Applicant argues that Chen's disclosure of PEO lipid bilayers, notwithstanding a citation to reference 59 of the reference of Chen, (i.e., Dori et al., Ligand accessibility as means to control cell response to bioactive bilayer membranes, Journal of Biomedical Materials Research, 2000.50(1): p. 75-81, (IDS filed5/26/2005)), (which applicant alleges does not even appear to discuss a PEO lipid bilayer.

Response to Arguments

Applicant's arguments entered 5/26/2005 have been fully considered but they are not persuasive.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., lipid bilayers floating within corrals) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Claims must be given their broadest reasonable interpretation consistent with the supporting description. In re Hyatt, 211 F.3d 1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000). The instant claims are drawn to lipids and so encompass the PEO lipid

bilayers, as taught by Chen, even if the claims do not specifically exclude PEO lipid bilayers, and even if the instant specification does not teach PEO lipid bilayers.

In fact, the reference of Chen teaches lipid bilayers. For example, Chen states:

> [0102] The methods described herein enable the customization of cell culture environments for cell and tissue and engineering. The combination of microfluidic and photolithographic patterning as well as simple adsorption of adhesive (ECM) and non-adhesive (PEO) species can be extended to novel applications such as: modification of the PPO Pluronic core with adhesive peptides to create surfaces with well-defined adhesivity [25], use of degradable triblocks (PEO-PLGA-PEO) to dynamically modulate adhesivity [58], and novel substrates such as ***PEO lipid bilayers*** [59] and biomaterials (PLGA)[43]. Furthermore, the patterning modes utilized can be used in microcontact printing of proteins [60-62] and microfluidics with polymer or hydrogel actuation [28,63]. [Emphasis added].

Chen et al., at para [0102].

Reference 59 of the reference of Chen, i.e., Dori et al., Ligand accessibility as means to control cell response to bioactive bilayer membranes, Journal of Biomedical Materials Research, 2000.50(1):p. 75-81, (IDS entered 5/26/2005), teaches cells adhesion to lipid bilayer membranes created by Langmuir-Blodgett deposition of either a pure poly(ethylene glycol) lipid having head groups of various lengths or binary mixtures of a poly(ethylene glycol) lipid and a novel collagen-like peptide amphiphile on a hydrophobic surface. As referred to by Chen, the reference of Dori et al., teaches cell adhesion to a lipid bilayer membrane (see, e.g., Dori et al., throughout the publication and abstract, and especially Figures 4 and 5). A reasonable reading of the reference of Chen is that Chen contemplates using PEO lipids in the lipid bilayer membranes further taught by Dori et al.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

9. Claims 7-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al., U.S. Publication No. 2002/0182633 and Boxer et al., U.S. Patent No. 6,228,326, (IDS filed 5/15/2002). This rejection maintains the reasons of record, as set forth in the previous Office action.

The claims are drawn to methods for screening, determining or observing living cell adhesion comprising providing a micro-array device comprising membranes in corrals, contacting or culturing cells in the device, and determining adhesion of the cells to the membranes; and wherein the membranes are lipid bilayers, wherein the membranes are posed with negatively or positively charged lipids, wherein the membranes are separated from a solid substrate by a later layer, wherein the substrate is a micropatterned glass wafer; wherein the membrane is an egg-phosphatidylcholine membrane; wherein the lipid is phosphatidylserine (elected species).

Chen et al., U.S. Publication No. 2002/0182633, throughout the publication, and especially at para [0012], at teach methods of observing and screening cell adhesivity or attachment, comprising biomolecules, including lipids, (specification at para [0022], [0066]) on glass substrates for use in microarray analysis; at para [0073] wherein the spatially patterned surfaces have areas that are adhesive to cells and areas that do not bind cells, and wherein the cell adhesive areas form islands that are isolated by cytophobic regions to which cells do not adhere (reading on corrals and barriers) and wherein the islands may have a lateral dimension of between 0.2 and 10 microns; at para [0102], teach lipid bilayers; at para [0109] teach allowing cells to attach for 2 hours; at para [0123] teach the visual assays for determining cell adhesion; and at para [0119] teach using glass wafers as supports.

The reference of Chen et al., does not disclose methods wherein the membranes of the micro-array are doped with negatively or positively charged lipids, the solid substrate is separated from the membranes by a water layer, wherein the membrane is an egg-phosphatidylcholine membrane; wherein the membrane comprises a lipid that is phosphatidylserine (elected species).

Boxer et al., U.S. Patent No. 6,228,326, throughout the patent and especially at col. 3, lines 28-col. 4, line 43, and col. 7, lines 50-61, teach devices having a surface defining a plurality of distinct bilayer-compatible surface regions separated by bilayer barrier regions that are corrals, and wherein the bilayers are carried on an aqueous film between the surface and the lipid bilayer; wherein the lipid bilayer expanse comprises phosphatidylserine and phosphatidylcholine; wherein the bilayer surface; at col. 8, lines 11-col. 53, teach support material microfabricated from a wafer of silicon, and wherein corrals are 5 micron square corrals; at col. 8, line 61-col. 9, line 20, teach egg phosphatidylcholine- cholesterol vesicles for preparing lipid bilayers via vesicle fusion; at col. 20, lines 15-21, teach egg phosphatidylcholine, and the fluorescent probe N-(Texas Red sulfonyl)-1,2-dihexadecanoyl-sn-glycero-3-phosphoethanolamine, triethylammonium salt. Boxer et al., at col. 21, lines 56-67, teach barriers to lateral diffusion, preventing mixing between fluid membranes in separate corrals.

It would have been prima facie obvious at the time the invention was made for one of ordinary skill in the are to have used methods of screening or determining cell adhesion, wherein the membranes of the micro-array are doped with negatively or positively charged lipids, the solid substrate is separated from the membranes by a water layer, wherein the membrane is an egg-phosphatidylcholine membrane; and wherein the membrane comprises a lipid that is phosphatidylserine.

One of ordinary skill in the art would have been motivated to use methods for screening or determining cell adhesion because Chen et al. teach using methods for determining cell adhesion in order to control cell-surface interactions; and because Boxer et al. teach doping cell membranes with negatively charged, fluorescent lipids as markers to characterize the fluidity of membranes; because Boxer et al. teach membranes that are separated from the solid support by a water layer are produced by using fusion of vesicles to form lipid bilayer membranes, as taught in the art; membranes that are egg-phosphatidylcholine are long known in the art as a component for artificial lipid bilayer membranes; and membranes comprising phosphatidylserine because phosphatidylserine is a lipid well known for synthetic and natural vesicles.

One of ordinary skill in the arts would have had a reasonable expectation of success in using methods used methods of screening or determining cell adhesion, wherein the membranes of the micro-array are doped with negatively or positively charged lipids, the solid substrate is separated from the membranes by a water layer, wherein the membrane is an egg-phosphatidylcholine membrane; and wherein the membrane comprises a lipid that is phosphatidylserine, because artificial membranes doped with charged lipids, natural membranes containing egg-phosphatidylcholine and synthetic or natural membranes comprising the lipid phosphatidylserine represent standard technologies that are well known in the art.

Applicant argues that PEO lipid bilayers, as taught by the reference of Chen, are not claimed in the applicant's application. Conversely, the applicant's lipid bilayers floating within corrals are not described by the reference of Chen. Instead, Chen et al. generally appears to bind selectively only directly to substrates, not to any lipid bilayers. Applicant argues that Chen's disclosure of PEO lipid bilayers, with a citation to reference 59 of the reference of Chen, (i.e., Dori et al., Ligand accessibility as means to control cell response to bioactive bilayer membranes, Journal of Biomedical Materials Research, 2000.50(1): p. 75-81, (IDS filed5/26/2005)), does not appear to discuss a PEO lipid bilayer.

Applicant argues that because Chen only refers to PEO monolayers, Chen does not appear to provide motivation to use lipid bilayers. Second, Chen's PEO monolayers have only been shown to prevent protein absorption and so Chen directly teach away from the claimed invention, or does not refer to adsorption of cells in any way. Third Chen's PEO monolayers would appear to have been directly deposited on the substrate

and are not comparable to applicant's micro-arrays of lipid bilayer members, as one cannot deposit a lipid monolayer over a water layer, and so using Chen's PEO monolayers with the Boxer et al. patent would have no reasonable expectation of success. Fourth Chen's prevention of cell adsorption directly teaches away from applicant's claim 7.b limitation of observing cell adhesion, and therefore would have not expectation of success. Additionally, the rigidly static lipid, even if Chen had taught it would have only remove similarity to dynamic lipid bilayer membranes.

Applicant argues that the reference of Boxer fails to teach the binding of cells to a lipid bilayer. Applicant argues the Boxer reference essentially states that a usable lipid bilayer membrane over a water layer will exhibit fluorescence recovery after photobleaching (FRAP) recovery. Any layer using the teaching of Chen would fail to exhibit FRAP recovery as the layers would be bound to the substrate and hence static. As Chen teaches of layers bound to the substrate and Boxer teaches a lipid bilayer supported by a water layer that has a fluid or dynamic nature, both references teach opposing techniques and there would be no reasonable expectation of success in such an unlikely combination.

Response to Arguments

Applicant's arguments entered 5/26/2005 have been fully considered but they are not persuasive.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., lipid bilayers floating within corrals) are not recited in the rejected claim(s).

Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Claims must be given their broadest reasonable interpretation consistent with the supporting description. In re Hyatt, 211 F.3d 1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000). The instant claims are drawn to lipids and so encompass the PEO lipid bilayers, as taught by Chen, even if the claims do not specifically exclude PEO lipid bilayers, and even if the instant specification does not teach PEO lipid bilayers.

In fact, the reference of Chen teaches lipid bilayers. For example, Chen states:

> [0102] The methods described herein enable the customization of cell culture environments for cell and tissue and engineering. The combination of microfluidic and photolithographic patterning as well as simple adsorption of adhesive (ECM) and non-adhesive (PEO) species can be extended to novel applications such as: modification of the PPO Pluronic core with adhesive peptides to create surfaces with well-defined adhesivity [25], use of degradable triblocks (PEO-PLGA-PEO) to dynamically modulate adhesivity [58], and novel substrates such as ***PEO lipid bilayers*** [59] and biomaterials (PLGA)[43]. Furthermore, the patterning modes utilized can be used in microcontact printing of proteins [60-62] and microfluidics with polymer or hydrogel actuation [28,63]. [Emphasis added].

Chen et al., at para [0102].

Reference 59 of the reference of Chen, i.e., Dori et al., Ligand accessibility as means to control cell response to bioactive bilayer membranes, Journal of Biomedical Materials Research, 2000.50(1): p. 75-81, (IDS entered 5/26/2005), teaches cells adhesion to lipid bilayer membranes created by Langmuir-Blodgett deposition of either a pure poly(ethylene glycol) lipid having head groups of various lengths or binary mixtures of a poly(ethylene glycol) lipid and a novel collagen-like peptide amphiphile on a

hydrophobic surface. As referred to by Chen, the reference of Dori et al., teaches cell adhesion to a lipid bilayer membrane (see, e.g., Dori et al., throughout the publication and abstract, and especially Figures 4 and 5). A reasonable reading of the reference of Chen is that Chen contemplates using PEO lipids in the lipid bilayer membranes further taught by Dori et al.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

One ordinary skill in the art would have had a reasonable expectation of success in combining the references of Chen and Boxer and would have been motivated to use methods comprising lipid bilayers, because the reference of Chen et al. states that their methods enable customization of cell culture environments for cell and tissue engineering, through the extension of microfluidic, photolithographic patterning, and cell adhesion molecules, to applications involving modulation of adhesivity and lipid bilayer substrates.

The reference of Boxer et al. teaches that cell adhesion to planar membranes was long known in the art (e.g., col. 9, 4-12). Boxer contemplates the production of membranes that behave as cell membranes (col. 15, line 65-col. 16, line 7). As set forth in the previous Office action, Boxer teaches devices having a surface defining a plurality of distinct bilayer-compatible surface regions separated by bilayer barrier regions that

are corrals, and wherein the bilayers are carried on an aqueous film between the surface and the lipid bilayer; and wherein the lipid bilayer expanse comprises phosphatidylserine and phosphatidylcholine.

The reference of Chen et al. teaches extension of their methods to lipid bilayers. The examiner respectfully submits that the reference of Chen et al. does not indicate that such lipid bilayers would not work with their invention (see above). Boxer et al. teach variously formulated lipid bilayer planar membranes. Both Chen and Boxer are concerned with the art of cellular membrane adhesivity. Applicant does not indicate how a *combination* of the teachings of the Chen and Boxer references would not have a reasonable expectation of success, especially when the adhesion of cells to a lipid bilayer membrane was known in the art.

Conclusion

10. Claims 7-20 are rejected.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Shibuya whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark L. Shibuya
Examiner
Art Unit 1639

ms

PADMASHRI PONNALURI
PRIMARY EXAMINER